Staphylococcal Infections in Infants

Updates and Current Challenges

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KEYWORDS

• Coagulase-negative staphylococci • *Staphylococcus aureus* • Infants • Neonatal intensive care unit • Sepsis • Bloodstream infection • Resistance • Heteroresistance

KEY POINTS

- Staphylococci are a leading cause of late-onset sepsis in infants.
- Coagulase-negative staphylococcal definition needs harmonization.
- Emergence of antibiotic resistance affects choice of empirical antibiotic therapy.

INTRODUCTION

Staphylococci are common pathogens in the neonatal period, especially after 3 days of life, causing up to 90% of late-onset sepsis (LOS) in hospitalized infants.[1,2] *Staphylococcus aureus* (SA) represents around 10% of LOS, whereas the proportion of coagulase-negative staphylococci (CoNS) ranges from 30% to 60%.[1,3,4] Variability in rates of CoNS sepsis is partly explained by inconsistent definitions in the literature and clinical practice. Establishing the diagnosis of a CoNS sepsis is challenging, because of the difficulty in discriminating culture contamination from true infection.

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Staphylococcal infections are associated with prolonged hospitalization, mortality, and neurodevelopmental impairment (NDI).[5] Treatment is increasingly complicated by the emergence of antibiotic resistance. The prevalence of methicillin-resistant SA (MRSA) has been reported as less than 1% to 8% among all infants in neonatal intensive care units (NICUs), with wide variations across NICUs,[6,7] and more recently, the emergence of vancomycin resistance in SA and CoNS has challenged treatment even further,[8–10] especially in infants for whom safety and effectiveness of new antistaphylococcal drugs are not well established.

In this article, the changing epidemiology and the challenges of diagnosing and treating neonatal staphylococcal infections in the NICUs are discussed. A better understanding of the current data will help optimize management of infants and identify areas of prevention and future research.

EPIDEMIOLOGY

Humans are the principal reservoir of staphylococci. Staphylococcal acquisition occurs directly via contact of hands or body fluids from colonized individuals.[11] Transmission can also occur via indirect contact of colonized objects including stethoscopes, clothing, and equipment.[11] Staphylococci from the infant's skin may cause infection, typically after disruption of the skin or integrity of the mucosal membranes with catheters and tubes.[11] It has been suggested since the 1960s that health care workers are a major source of staphylococcal infection, but recent data have shown that maternal colonization also increases the risk of newborn staphylococcal colonization, through vertical transmission and breastfeeding.[12,13]

Staphylococcus aureus

Prevalence/incidence and risk factors

SA frequently colonizes infants, with up to 50% colonization rates in the first days of life.[1,14–16] SA is a rare cause of early-onset sepsis (EOS) (<1%) and responsible for 8% to 15% of LOS.[4] Over a period of 10 years, a study[16] showed a slight but significant increase in SA bacteremia (0.91% in 2000–2003 and 1.73% in 2004–2009, $P<.001$) in the NICU.

MRSA is an increasing concern, representing up to 55% of SA infections in NICUs.[16–19] MRSA incidence is increasing as reported by the Centers for Disease Control and Prevention's (CDC) National Nosocomial Infections Surveillance system (0.7–3.1 per 10,000 infants infected from 1995 to 2004).[19] Thirty percent of participating NICUs had no MRSA infections, indicating that differences in geographic location, hospital-specific infection control policy, and compliance to preventive measures may contribute to variation in infection rates.[19]

Infants with MRSA and meticillin-susceptible SA (MSSA) infection were shown to have similar gestational age (GA) and birth weight (BW).[20,21] However, those with MRSA infection tended to be younger at time of diagnosis compared with those with MSSA (median age of 23 vs 32 days, $P = .03$).[20] In addition to postnatal age, MRSA colonization was also shown to increase the risk of MRSA infection (relative risk: 2.64; 95% confidence interval [CI]: 2.34–2.98).[6]

Outcomes

Overall, SA-related mortality ranges from 5% to 18%, but it is as high as 25% in very low BW infants (VLBW; <1500 g BW).[14,16,18,21,22] In a study conducted in 20 US NICUs,[14] MRSA and MSSA infections were associated with similar mortality (26% and 24%, respectively) and morbidity in VLBW infants. In contrast, a study including all infants admitted to 17 Australian NICUs[22] observed a higher